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1. A programmable, conditionally activatable small interfering RNA (Cond-siRNA) construct comprising a sensor strand, a core strand, and a guide strand, wherein:

(i) the sensor strand and the core strand form a sensor duplex,

(ii) the guide strand and the core strand form a RNAi duplex, and

(iii) the sensor duplex is attached to the RNAi duplex to form a single structure.

2. The Cond-siRNA construct of claim **1**, wherein the sensor strand has an overhang that is not complementary to the core strand, and wherein the overhang on the sensor strand is capable of complementary binding to an input strand to form a toehold, thereby causing the displacement of the sensor strand from the core strand.

3. The Cond-siRNA construct of claim **1**, comprising one or more of the following chemical modifications:

A. the use of a sensor strand where the highlighted area A has one or more of the following features:

a. 50% or less of the backbone positions are phosphorothioate (PS) connections;

b. 50% or more of the bases are chemically modified to resist nuclease degradation or increase the melting temperature of the duplex (Tm);

c. 100% of the bases are chemically modified to resist nuclease degradation and increase Tm; and

d. about 10%-50% of the bases are locked nucleic acid (LNA) or other chemically modified base with 2'-4' bridging modifications that substantively increase the Tm;